(19)日本国特許庁（ＪＰ）　(12)公開特許公報（Ａ）　(11)特許出願公開番号

特開平9－227410

(43)公開日　平成９年(1997)９月２日

(51)Int.Cl.[6]		識別記号	庁内整理番号	ＦＩ		技術表示箇所
Ａ６１Ｋ	45/00	ＡＥＤ		Ａ６１Ｋ	45/00	ＡＥＤ
	31/70				31/70	
	38/00				39/395	Ｄ
	39/395					ＡＢＣＮ
		ＡＢＣ			37/02	

審査請求　未請求　請求項の数４　ＦＤ　（全５頁）

(21)出願番号　特願平8－60123

(22)出願日　平成８年(1996)２月21日

特許法第30条第１項適用申請有り　平成７年９月１日　財団法人循環器病研究振興財団法人発行の「研究助成業績報告集　1994（平成６）年度」に発表

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(54)【発明の名称】　臓器移植拒絶反応の抑制剤

(57)【要約】
【課題】臓器移植拒絶反応を抑制するための薬剤の提供。
【解決手段】Ｐ－セレクチンの結合阻害剤を含有する臓器移植拒絶反応の抑制剤。例えば、Ｐ－セレクチンの結合阻害剤として抗Ｐ－セレクチン抗体を含有する該抑制剤。

PATENT ABSTRACTS OF JAPAN

(11)Publication number : 09-227410

(43)Date of publication of application : 02.09.1997

(51)Int.Cl. A61K 45/00
A61K 31/70
A61K 38/00
A61K 39/395
A61K 39/395

(21)Application number : 08-060123

(22)Date of filing : 21.02.1996

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(54) SUPPRESSANT FOR REJECTION IN ORGAN TRANSPLANTATION

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain a suppressant for rejection in organ transportation, comprising a bonding inhibitor for P-selectin as an active ingredient, capable of preventing the accumulation of leukocytes caused at the time of organ transplantation and subsequent activation thereof and effective against rejection in the organ transplantation.

SOLUTION: This suppressant for rejection in organ transplantation comprises a bonding inhibitor of P-selectin, preferably an anti-P-selectin antibody, a ligand of the P-selectin or an antibody specific for the ligand of the P-selectin, P- selectin or its fragment, a biosynthetic inhibitor of the ligand of the P-selectin or an inhibitor of the expression of the P-selectin as an active ingredient. Furthermore, the dose of the suppressant is about 0.5mg to about 1g for, e.g. a patient weighing 70kg.

LEGAL STATUS

[Date of request for examination]

[Date of sending the examiner's decision of rejection]

[Kind of final disposal of application other than the examiner's decision of rejection or application converted registration]

[Date of final disposal for application]

[Patent number]

[Date of registration]

[Number of appeal against examiner's decision of rejection]

[Date of requesting appeal against examiner's decision of rejection]

[Date of extinction of right]

JP-A-9-227410

Claim(s):

[Claim 1] An inhibitor of organ transplantation rejection which contains as an active component an inhibitor of binding to P-Selectin.

[Claim 2] The inhibitor according to claim 1, wherein said inhibitor of binding to P-Selectin is anti-P-Selectin antibody, a ligand of P-Selectin or its derivative, an antibody specific for the ligand of P-Selectin , P-Selectin or its fragment, a inhibitor of biosynthesis of the ligand of P-Selectin , or a inhibitor of expression of P-Selectin.

[Claim 3] The inhibitor according to claim 1, wherein said inhibitor of binding to P-Selectin is anti-P-Selectin antibody.

[Claim 4] The inhibitor of any one of claims 1 to 3, wherein the organ transplantation is a heart transplantation.

[0002]

[Description of the Prior Art]

When an organ lapses into a malfunction according to various critical diseases, transplanting other human' organ as the cure is performed. Recently, the attempt which transplants the organ of an animal to human has also started. In the organ transplantation to this human, rejection poses a problem most on clinical. This will drop out without the ability carrying out the take of the organ (graft) transplanted to the near (recipient) body which receives transplantation. The allograft immunoreaction is thought in the first place as a cause of the rejection. If matter other than a self component invades in the living body, a living body is going to recognize the matter as an antigen, and eliminate a foreign

matter by the cellular immunity by the lymphocyte, and the humoral immunity by the produced antibody as part of self-defense. In the transplantation immunity reaction, a recipient recognizes a graft as an antigen and is considered that refusal is performed by the immunoreaction of the T cell subject who shows a series of cascades called activation of a T cell and growth, and destruction of a graft. therefore, a group called an immunosuppresant in the case of an organ transplantation in order to suppress this reaction -- the drug is used. There are corticosteroid (prednisone) and cyclosporin A in them, and, recently, FK-506 came to be further used widely. However, if the effectiveness of these drugs is also perfect, there is nothing, and the side effect is also reported. The cause considered by the second is an ischemia reperfusion failure. Blood is resumed by transplantation to a recipient after, as for a graft, a blood flow is temporarily intercepted with the extraction on the occasion of an organ transplantation (ischemia) (reperfusion). By ischemia-reperfusion actuation, it is known well that the organization of a reperfusion part will receive a failure, and it is thought that activation of the neutrophil leucocyte contained in blood is involving as at least one of the operation mechanism of this. That is, in the animal experiment, it is shown clearly for the animal which decreased neutrophil leucocyte that a reperfusion failure is mitigated sharply. Therefore, controlling activation of a leucocyte by a certain approach prevents an ischemia reperfusion failure, and it is considered to be the effective means of the organ derangement prevention at the time of an organ transplantation.

[0004]

[Problem(s) to be Solved by the Invention]

An object of this invention is, by preventing accumulation of the leucocyte produced at the time of an organ transplantation, and the activation which follows it to find out the drugs, to prevent the rejection of an organ transplantation.

[0010]

The ligand of P-selectin, and its derivative include glycoprotein, glycolipids, and oligosaccharides as terminal structures thereof, which are on the surface of leucocyte, and the derivatives thereof. For example, as oligosaccharide and its derivative, sialyl-Lewis x and sialyl-Lewis x derivative, Lewis x and Lewis x derivative, sialyl-Lewis a and sialyl-Lewis a derivative, Lewis a and Lewis a derivative, sulfated sugar, phosphorylated sugar, sulfatide, and so on (for example, Varki et al. Proc. Natl. Acad. Sci. USA 91, 7390 (1994), WO 94/26760). As an example of glycoprotein, PSGL-1 (for example, Sako et al. Cell 75, 1179 (1993)) etc. can be cited.

[0011]

An antibody specific for the ligand of P-Selectin means a antibody specific for the ligand mentioned above. The antibody may be either a polyclonal antibody or a monoclonal antibody. Although the origin of this antibody is not restricted, antibodies from mouse or human, chimera antibodies which combined parts of both the antibody from a mouse or human, and anthropomorphized antibody can be cited. Specifically, anti-sialyl-Lewis x antibody, anti-sialyl-Lewis a antibody, anti-Lewis X-antibody, anti-Lewis a-antibody, etc. may be cited (for example,

Fukushima et al. Cancer Res. 44, 5279 (1984), Shitara et al. Cancer Res. 47, 1267 (1987), Takada et al. Biochem. Biophys. Res. Commun. 179,713 (1991)).